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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HAMUD, FOZIA M	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 05/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/807,558	ANKER ET AL.	
	Examiner	Art Unit	
	Fozia M. Hamud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27 and 29-31* is/are pending in the application.

4a) Of the above claim(s) *5-18 and 20-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,19 and 29-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 November 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/22/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

PD

Response to Amendment

1a. Receipt of Applicant's amendment and arguments, filed on 03 November 2004, is acknowledged.

Status of Claims:

1b. Originally claims 1-47 have been filed, of which Claims 28 and 32-47 have been cancelled. Thus, claims 1-27, 29-31 are pending, of which claims 1-4, 19, 29-31 are under consideration. Claims 5-18, 20-27 stand withdrawn, however, in the event that the any of the generic linking claims 1, 29-31, become allowable, claims which depend upon and include all the limitations of the allowable claims will be considered for rejoinder. Furthermore, should the rejoined claim be drawn to different inventions, the restriction requirement between the elected invention and the rejoined inventions will be withdrawn.

1c. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Petition Decision* and *Election/Restriction:

2a. The petition filed on 06 July 2004, under 37 C.F.R 1.181 has been granted in part. The petition was found persuasive regarding the identification and treatment of linking claims. Therefore, should any of the generic linking claims 1, 29-31, are found allowable, claims which depend upon and include all the limitations of the allowable claims will be considered for rejoinder. Should the rejoined claims be drawn to different inventions, the restriction requirement between the elected invention and the rejoined inventions will be withdrawn. Accordingly, the objection to claim 2 is withdrawn.

Furthermore, search and examination of the generic linking claims 1, 29-31 will not be limited to the elected invention.

3. The following previous objections are withdrawn in light of Applicants amendments filed on 11/03/04:

(i) The objection of claim 2 is withdrawn, because this claim depends from generic linking claim 1.

Specification:

4a. The substitute specifications filed 02/10/05 and 11/03/04 have not been entered because they do not conform to 37 CFR 1.125(b) and (c) because:

The filing of two substitute specifications renders the examination of the instant case difficult. The clean version of the substitute specification filed on 11/03/04 comprises 45 pages, while the clean version of the one filed on 02/10/05 comprises 43 pages. It is unclear what changes are being made. Furthermore, the substitute specifications filed on 11/03/04 deletes four examples, without any reasoning or rationale. The substitute specifications filed on 02/10/05 indicates that figures 3 and 4 are deleted, however, these figures are still part of the drawings. Therefore, the substitute specifications filed on 02/10/05 and 11/03/04 are considerably different from the originally filed specification. Thus, it very difficult to decipher what changes are being made in which substitute specification.

Furthermore, the deletion of examples 6 through 9 from the originally filed specification, is objected to under 35 U.S.C. 132(a), because it introduces new matter.

These deletions change the content and substance of the specification, such that contemplation is not of the same scope.

Brief Description of the Drawings:

4b. There are 4 new figures in the instant case, however, the brief description of the figures describe only two figures. Furthermore, the description of figures 1 and 2 in the specification, does not seem to correlate with figures 1 and 2. For example, figure 1 supposedly marks plasma levels of noradrenaline that is higher than normal with an (*), however, there is no such marking on the figure. The description of figure 2 does not match the figure. The instant specification fails to provide description for figures 3 and 4.

4c. Original Figure 1 has been converted into a Table A, however, no meaningful data can be discerned from this table. Firstly, there are three tables included within this table. Secondly, the heading of the table indicates that plasma levels of noradrenaline are being measured, however, sub-headings cite "HA in nmol/l", and it is unclear what the abbreviation HA stands for and what is being measured. Clarification of what is being measured in Table A is required.

Drawings:

5a. The drawings stand objected to. Applicants have filed new Figures 1-4 on 09 November 2005. Original Figure 1 has been converted into a Table A, and original Figures 2-5 are now figures 1-4, respectively. However, Applicants failed to label new figures 1, 2 and 4 properly. The Y axis of figure 1 is not labeled, therefore, it is unclear what is being measured. Regarding figure 2, the title of the graph indicates that this is a

plot for aldosterone ng/ml, however, the Y axis is labeled as Cell Mean. Thus, it is unclear whether the cell number is measured or aldosterone in ng/ml. Figure 4 is not labeled. Appropriate correction is required.

Claim rejections-35 USC § 112:

6a. Claims 1-4, 19, 29-31 stand rejected under 35 U.S.C. 112, first paragraph, for reasons of record set forth in the office action mailed on 03 May 2004, pages 7-11.

Applicants argue that the courts have described the legal standard for enablement under 112, first paragraph, as whether one skilled in the art could make and use the claimed invention from the disclosures in the patent application coupled with information known in the art. Applicants cite numerous case laws that support this point. Applicants emphasize the fact that some experimentation is necessary does not preclude enablement and that there is no requirement for examples. Applicants contend that a common mechanism leads to cachexia in a number of patients with different diseases, such that cachexia can be treated with drugs that are functionally related by their ability to decrease SNS activity. Applicants argue that the specification demonstrates that patients with weight loss due to a number of diseases have elevated noraddrenaline plasma levels, compared to controls. Applicants also point out that figures 3 and 4 of the instant specification disclose that aldosterone and angiotensin II levels are also elevated in cachectic subjects. Thus, applicants conclude that since cachectic patients show similar hormonal profile, that weight loss can be treated with agents disclosed on pages 4 to 13 of the instant specification. Applicants argue that all of these compounds are known (although not for the treatment of cachexia) in the art

with established mechanisms of action, and all affect sympathetic nervous system activity, and are therefore, related through this common action. Applicants conclude that it would be routine to select a suitable agent and a suitable dose for the treatment of cachexia. Applicants also submit that the prior art acknowledges that 400 mg daily of Spironolactone is safe, therefore, that 12.5 to 300 mg/day disclosed in the instant specification safe. Applicants also submit that the initial weight loss observed by RALES study with 75 mg of spironolactone is entirely consistent with the diuretic activity of the drug. Applicants submit several references that allegedly support that the claimed invention is enabled.

(Although applicants arguments' are based on limitations not recited in any of the instant claims, namely, cachexia. Stedman's Medical Dictionary 27th Edition describes cachexia, as weight loss and wasting occurring in the course of a chronic disease or emotional disturbance.)

Applicants' arguments have been considered fully, but are not deemed persuasive. It is not disputed that a claimed invention is enabled so long as one skilled in the art could make and use said invention from the disclosures in the patent application coupled with information known in the art. In the instant case, the claims are not enabled to their full scope. The instant specification is only enabling for a method of treating chronic heart failure (CHF) by administering spironolactone. However, the instant specification does not provide enablement commensurate in scope for a method of treating weight loss due to *underlying disease* by administering to the patient an agent that reduces sympathetic nervous system. Also the fact pattern of the cases cited

by Applicants are different than what is disclosed in the instant specification. It is agreed that the specification need not disclose what is well known in the art, but, this only means that the omission of minor details which does not cause the specification to meet the enablement disclosure. However, the courts have held that when there is no disclosure of any starting material or any conditions under which a process can be carried out, undue experimentation is required. Thus, it is the specification, not the knowledge of the skilled artisan that should supply the novel aspects of the claimed invention, in order to satisfy the enablement requirement, (Genetech, inc v. novo nordisk 42 USPQ2Dd at 1004). In the instant case, a common mechanism is speculated for causing cachexia, however, the specification fails to provide reasonable detail to enable the skilled artisan to practice the claimed invention. The instant specification only establishes that aldosterone, angiotensin II and noraddrenaline levels are elevated in patients suffering from the diseases listed in claim 29. There is no disclosure, for example, of an AIDS patient, a cancer patient, a malnourished patient or a patient with renal failure that was treated with an agent that reduces SNS activity. Although working examples are not necessary for enablement under 112, first paragraph, they are one of the factors to be considered, when evaluating enablement requirements. In the instant case, the instant specification fails to disclose specific drugs, dosage, regimen or results, for the claimed method. Applicants admit that the drugs recited on pages 4-13 of the instant specification, are known in the art, although they are not known for treating cachexia. Therefore, contrary to Applicants' argument, it will not be routine to select a suitable agent and a suitable dose for the treatment of

cachexia, because this is the novel aspect of the invention and applicant must provide details of how to carry it. Furthermore, since the patient to be treated for the weight loss obviously has an underlying disease, the treatment for the weight loss has to be correlated with the treatment of said underlying disease. The drugs to be used for the treatment of the weight loss must be compatible with the other medications that the patient is taking. However, the instant specification does not address this issue. Furthermore, although the specification discloses the administration of spironolactone to a patient having chronic heart failure (CHF), the specification does not treat patients that suffer from any of the other diseases recited in claim 29. Regarding the safety of spironolactone, the prior art recognizes that this drug is safe at 400 mg daily for the treatment of refractory edema associated with heart failure. However, the instant specification does not disclose nor prior art teach whether, the dosages recited in the instant specification (12.5 to 300 mg/day), are safe for "all possible" patients that suffer from weight loss due to "all possible" underlying diseases. Again the interaction of all the medications that a specific patient is taking must be considered in order to address the safety of any new drug for said patient.

All of the submitted references have been considered. As was set forth in the previous office action, the instant specification a method of treating chronic heart failure (CHF) by administering spironolactone. Coats et al disclose a method of reversing cardiac cachexia in patients with severe heart failure by administering Carvedilol. Carvedilol is a beta adrenergic blocking agent that is used for the treatment of heart failure. Hryniewicz et al disclose the reversal of cahcexia by administering beta

adrengeric receptor blocker. These references use specific class of drugs known to be used for the treatment congestive heart failure, and show that they reverse the cachexia caused by this specific disease. However, neither the instant specification nor the prior art teach that these drugs would also reverse cachexia caused by other disorders, for example, AIDS or emotional disturbance.

Therefore, the instant specification is only enabling for a method of treating chronic heart failure (CHF) by administering spironolactone.

6b. Claims 1, 2, 3, 4, 19, stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for reasons of record set forth in the office action mailed on 03 May 2004. Applicants argue that the written description for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice. Applicants argue that they discovered a common mechanism leads to cachexia in a number of patients. Thus, the skilled artisan would know to select a suitable compound that reduces the sympathetic nervous system. Applicants argue that to limit the claims to the compounds recited in claim 4 is improper, since a large number of compounds reduce SNS activity. Applicants submit that the compounds recited on pages 4, 8 and 13 of the instant specification are well known in the art and may have been used in humans. Applicants conclude that the specification satisfies the written description by describing sufficient number of species by functional characteristics.

This argument is not found persuasive. The written description fail to satisfy "all possible" compounds that reduce SNS. The compounds recited on pages 4, 8 and 13 of

the instant specification do not satisfy the written description, because the claims describe the agents used by their action alone and there are no structural limitation recited in the claims. Furthermore, since there is no common structure for all of the encompassed agents and there is no one single art recognized class of compounds, the skilled artisan would not recognize that all of the encompassed compounds would be useful in the claimed method. The claims encompass yet to be discovered agents. Therefore, claims 1, 2, 3, 4 and 19 fail to satisfy the written description provision under 35 U.S.C. 112, first paragraph.

7a. Claims 1-4, 19, 29-31 stand rejected under 35 U.S.C § 102(b) as being anticipated by RALES investigators (October 1996), for reasons of record set forth in the office action mailed on 03 May 2004, pages 14-15.

Applicants argue that the instant claims recite a method of treating weight loss due to an underlying disease not the disease itself. Applicants contend that RALES reference does not teach or suggest selecting patients with cachexia, nor does it disclose any sort of weight gain from the treatments. Applicants submit that a patient with congestive heart failure may develop cachexia, but by no means do all patients with CHF automatically have cachexia. Thus, treatment for cachexia is not the same as treatment for the underlying disease. Applicants argue that inherency requires more that a mere possibility that the claimed result will occur, it requires a reasonable prediction of the result. The fact that some patients may experience some weight gain during treatment is not same as selecting those individuals that need weight gain.

These arguments are not found persuasive. Firstly, Applicants are arguing limitations not recited in the claims. Cachexia is not recited in any of the claims. Secondly, the RALES reference teaches the administration of spironolactone to patients, suffering from CHF. As acknowledged by Applicants, some CHF patients suffer from weight loss. The instant specification only discloses a patient suffering from CHF as a candidate for the claimed treatment. Thus, the population treated with spironolactone in the RALES study is the same population disclosed in the instant specification as being susceptible to experience weight loss. Moreover, all of the references relied upon by Applicants for enablement purposes, disclose reversal of cachexia due to chronic heart failure, (Coats et al and Hryniewicz et al). Regarding the inherency argument, the active step in the instant claims is the administration of an agent that reduces SNS activity, to a specific patient population. Thus, the population in the RALES study are treated with spironolactone (an agent which reduces SNS), and this population are cacheixa candidates (same patients as recited in claim 1), therefore, claimed invention is anticipated by RALES. The fact the this drug may have an effect on body weight is a newly discovered result of a known process directed to the same purpose, and this does not make the instant method patentable.

Therefore the RALES reference anticipates the instant claims 1-4, 19, 29-31.

Conclusion:

8. No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M. Hamud whose telephone number is (571) 272-0884. The examiner can normally be reached on Monday, Thursday-Friday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Fozia Hamud
Patent Examiner
Art Unit 1647
11 May 2005

JANET ANDRES
PRIMARY EXAMINER